PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In application of

Kozo AOKI, *et al.*

Docket No: Q67718

Appln. No.: 10/019,249

Group Art Unit: 1625

Confirmation No.: 1284

Examiner: Patricia L. MORRIS

Filed: June 5, 2002

For: BENZIMIDAZOLE COMPOUNDS AND MEDICAMENTS COMPRISING THE SAME

APPELLANTS' BRIEF ON APPEAL UNDER 37 C.F.R. § 1.192

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with the provisions of 37 C.F.R. § 1.192, Appellants submit the following:

I. REAL PARTY IN INTEREST

The real party in interest is the assignee, Fuji Photo Film Co., Ltd. of Kanagawa, Japan.

II. RELATED APPEALS AND INTERFERENCES

Appellants, Appellants' legal representative, and the Assignee in this application are not aware of any other appeals or interferences which will directly affect or be affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

This is an appeal from the Examiner's rejection of claims 1-12 and 21.

IV. STATUS OF AMENDMENTS

As indicated in the Advisory Action dated September 3, 2003, the Amendment filed on August 14, 2003, is entered upon filing this Appeal. There are no unentered Amendments of record.

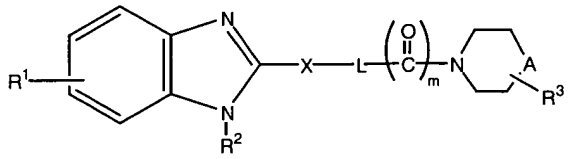
V. SUMMARY OF THE INVENTION

The present invention relates to a benzimidazole compound or a salt thereof having an inhibitory action of foaming of macrophages and is useful as an active ingredient of a preventive and/or therapeutic medicament of arterial sclerosis and hyperlipidemia. Specification, page 2, 1st full paragraph.

It is believed that foaming of macrophages plays a main role in the formation of arterial sclerosis lesions. Accordingly, suppression of the foaming of macrophages may possibly prevent arterial sclerosis by inhibiting the formation of arterial sclerosis lesions, or achieve radicular treatment of arterial sclerosis by retraction of arterial sclerosis lesions. Specification, page 1, 2nd full paragraph.

Although an inhibitor of ACAT reduces blood cholesterol levels and thus suppresses the foaming of macrophages in an animal experiment, it does not provide satisfactory inhibition of the foaming of macrophages. Specification, page 1, 3rd full paragraph.

Thus, an object of the present invention is to provide satisfactory suppression of the foaming of macrophages, and this object has been achieved by a benzimidazole compound which is represented by the following formula (I) or a salt thereof:



wherein, R^1 represents one or more functional groups on the benzene ring selected from the group consisting of a hydrogen atom, a halogen atom, a lower alkyl group, and a lower alkoxy group; R^2 represents a hydrogen atom, or an alkyl group; R^3 represents one or more functional groups on the ring containing the nitrogen atom and A; A represents CH_2, or CH which forms a double bond with an adjacent carbon atom; L represents a C_4-C_8 alkylene group or an ethyleneoxy linking group represented by $(CH_2CH_2O)_nCH_2CH_2$ wherein n represents 1 or 2; X represents O, S or methylene group; and m represents 0 or 1. Specification, paragraph bridging pages 2 and 3, and claim 1.

VI. ISSUES

The essential issue in this appeal is whether the Examiner has established a *prima facie* case of obviousness in rejecting claims 1-12 and 21 as obvious under 35 U.S.C. § 103(a) as over Giani et al (U.S. Pat. No. 4,971,980).

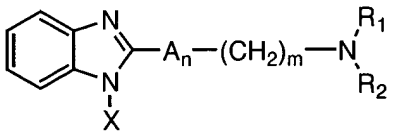
VII. GROUPING OF CLAIMS

Claims 1-12 and 21 are rejected as obvious under 35 U.S.C. § 103(a) as over Giani et al, and the claims do not stand or fall together for the reasons given herein, particularly with respect to the specific recitation of X in claim 2.

VIII. ARGUMENTS

The Examiner has not made a *prima facie* showing of obviousness of the claimed invention over Giani et al and therefore the rejection of claim 1-12 and 21 over Giani et al should be reversed.

Claims 1-12 and 21 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Giani et al. Giani et al teaches benzimidazole derivatives (I) having an antihistaminic activity, wherein A represents $-CH_2CH(CH_3)-$ or $-CH(CH_3)CH_2-$, n is 0 or 1; m represents 0 or an integer of from 1 to 5, X represents a radical selected from the group consisting of benzyl, fluorobenzyl, alkoxyalkyl and tetrahydrofurfuryl, R_1 and R_2 each represents a saturated or unsaturated alkyl radical, or they may form, together with the adjacent nitrogen atom, an optionally substituted heterocyclic ring selected from the group consisting of pyrrolidine and piperidine, and corresponding pharmaceutically acceptable acid salts. Abstract.



(I)

The compounds disclosed in Giani et al differ from the presently claimed compounds, at least as to the substituents at the nitrogen atom of the piperidine ring, that is, X in formula (I) of Giani et al and R^2 in formula (I) of the present invention.

In the Office Action dated May 14, 2003, the Examiner states that Giani et al teaches compounds homologous to the present invention, referring to Example 4 of Giani et al which has a C_4 alkylene chain. The Examiner also states that the compounds disclosed in Giani et al have pharmaceutical activity, and thus the skilled artisan would expect structurally similar compounds to possess similar properties.

Appellants respectfully submit that the Examiner has not established a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, there must be (1) some suggestion or motivation within the references or in the knowledge generally available to one of ordinary skill in the art to modify the reference; (2) a reasonable expectation of success; and (3) the prior art references must teach or suggest all of the claimed limitations. See *Hodesh v. Block Drug Co.,* 786 F.2d 1136, 1153, n.5, 229 USPQ 182, 187, n.5 (Fed. Cir. 1986); *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, 1438 (Fed. Cir. 1991); and *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). In this case, there is no reasonable expectation that compounds having a similar structure to Example 4 of Giani et al have pharmaceutical activities.

Specifically, as set forth in the Amendment Under 37 C.F.R. § 1.116 filed August 14, 2003, in Example 4 of Giani et al, 2-(4-piperidin-1-ylbutyl)benzimidazole was used as a starting material to prepare 1-(2-ethoxyethyl)-2-(4-piperidin-1-ylbutyl)benzimidazole, which is a compound having the general formula (I). However, 2-(4-piperidin-1-ylbutyl)benzimidazole itself does not meet the requirements of formula (I), because this compound has a hydrogen atom

at the position corresponding to X in formula (I). Further, there is no indication in Giani et al that 2-(4-piperidin-1-ylbutyl)benzimidazole itself has any pharmaceutical activity.

Therefore, even though 2-(4-piperidin-1-ylbutyl)benzimidazole might be characterized as a homologue of the presently claimed compounds, one of ordinary skill in the art would have no reason to use and modify this compound. Page 9, 2nd paragraph.

With respect to claim 2 in particular, Applicants submit that there is simply no teaching or suggestion in the art as to X being O or S in formula (I) of the present invention, so claim 2 is not obvious for this additional reason.

The Examiner has not rebutted Appellants' arguments above. Accordingly, Appellants respectfully requested reversal of the rejection of claims 1-12 and 21 as obvious under 35 U.S.C. § 103(a) over Giani et al.

IX. CONCLUSION

The present Brief on Appeal is being filed in triplicate. Unless a check is submitted herewith for the fee required under 37 C.F.R. §1.192(a) and 1.17(c), please charge said fee to Deposit Account No. 19-4880.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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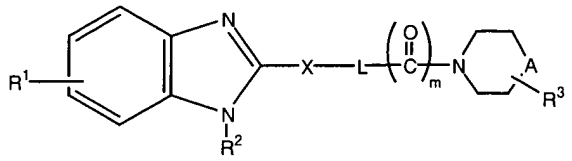
Date: December 8, 2003

APPENDIX

CLAIMS 1-12 and 21 ON APPEAL:

1. A benzimidazole compound represented by the following formula (I) or a salt thereof:



wherein, R^1 represents one or more functional groups on the benzene ring selected from the group consisting of a hydrogen atom, a halogen atom, a lower alkyl group, and a lower alkoxy group; R^2 represents a hydrogen atom, or an alkyl group; R^3 represents one or more functional groups on the ring containing the nitrogen atom and A; A represents CH_2, or CH which forms a double bond with an adjacent carbon atom; L represents a C_4-C_8 alkylene group or an ethyleneoxy linking group represented by $(CH_2CH_2O)_nCH_2CH_2$ wherein n represents 1 or 2; X represents O, S or methylene group; and m represents 0 or 1.

2. The compound or a salt thereof according to Claim 1, wherein X is O or S.

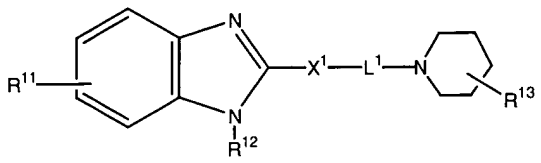
3. The compound or a salt thereof according to claim 1 or 2, wherein m is 0.

4. The compound or a salt thereof according to claim 1, wherein each of R^1 and R^2 represents a hydrogen atom.

5. The compound or a salt thereof according to claim 1, wherein L is a C_4-C_8 alkylene group.

6. The compound or a salt thereof according to claim 1, wherein L is a C_5 or C_6 alkylene group.

7. A benzimidazole compound represented by the following formula (II) or a salt thereof:



wherein, R^{11} represents one or more functional groups on the benzene ring selected from the group consisting of a hydrogen atom, a halogen atom, a lower alkyl group, and a lower alkoxy group; R^{12} represents a hydrogen atom, or an alkyl group; R^{13} represents one or more functional groups on the piperidine ring selected from the group consisting of a hydrogen atom, an alkyl group, a hydroxyalkyl group, a phenyl group which may be substituted, a hydroxyl group, an alkoxy group, an amino group, a cyano group, a carbamoyl group and an alkoxycarbonyl group; L^1 represents a C_4-C_8 alkylene group; and X represents O, S, or methylene group.

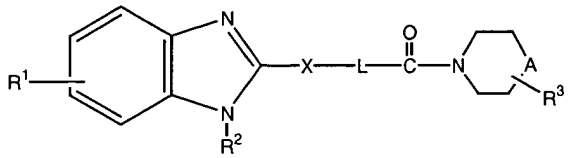
8. The compound or a salt thereof according to Claim 7, wherein L^1 is a C_4-C_8 alkylene group.

9. The compound or a salt thereof according to Claim 7 or 8, wherein R^{11} and R^{12} represent hydrogen atom.

10. The compound or a salt thereof according to claim 7, wherein R^{13} is a functional group selected from the group consisting of a hydrogen atom, an alkyl group, a hydroxyalkyl group, a phenyl group which may be substituted, a hydroxy group, and a cyano group.

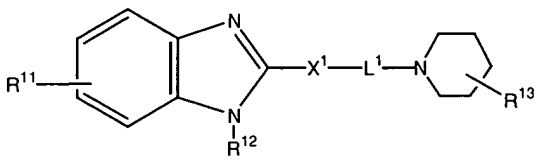
11. The compound or a salt thereof according to claim 7, wherein L^1 is a C_5 or C_6 alkylene group.

12. A pharmaceutical composition comprising a compound represented by the following formula (I)



wherein, R^1 represents one or more functional groups on the benzene ring selected from the group consisting of a hydrogen atom, a halogen atom, a lower alkyl group, and a lower alkoxy group; R^2 represents a hydrogen atom, or an alkyl group; R^3 represents one or more functional groups on the ring containing the nitrogen atom and A; A represents CH_2, or CH which forms a double bond with an adjacent carbon atom; L represents a C_4-C_8 alkylene group or an ethyleneoxy linking group represented by $(CH_2CH_2O)_nCH_2CH_2$ wherein n represents 1 or 2; X represents O, S or methylene group; and m represents 0 or 1, or a physiologically acceptable salt thereof as an active ingredient, and a pharmaceutical additive.

21. A pharmaceutical composition comprising a compound represented by the following formula (II)



wherein, R^{11} represents one or more functional groups on the benzene ring selected from the group consisting of a hydrogen atom, a halogen atom, a lower alkyl group, and a lower alkoxy group; R^{12} represents a hydrogen atom, or an alkyl group; R^{13} represents one or more functional groups on the piperidine ring selected from the group consisting of a hydrogen atom, an alkyl group, a hydroxyalkyl group, a phenyl group which may be substituted, a hydroxyl group, an alkoxy group, an amino group, a cyano group, a carbamoyl group and an alkoxycarbonyl group; L^1 represents a C_4-C_8 alkylene group; and X represents O, S, or methylene group, or a physiologically acceptable salt thereof as an active ingredient, and a pharmaceutical additive.